
# Synthesis and Antimicrobial Activity of Novel Heterocycles Containing Thiazolidinone and 1,3,4-Oxadiazole Moieties

## Tiazolidinon ve 1,3,4-Oksadiazol Payı İçeren Yeni Heterosiklik Maddelerin Sentezi ve Antimikrobiyal Etkinlikleri

Mannich Bases

K. Ranga Raju[1], B. Santosh Kumar[1], A. Raghavendra Guru Prasad[2], L.K. Ravindranath[1]
[1]Sri Krishnadevaraya University, Anantapur, A.P.,
[2]ICFAI Foundation for Higher Education, Hyderabad, A.P., India.

**Özet**

Amaç: Yeni 7-(4-((değişitirilmiş)5-tiokso-4,5-dihidro-1,3,4-oksadiazol-2-il) methyl) -4- (fenilamino)- 9(triklorometil)-1 -tia-4,7,8-triazaspiro[4.4] non-ene 3, 6-dion serisini tasarımlamak, sentezlemek ve karakterizasyon ve anti bakteriyel aktivitesi açısından incelemek. Gereç ve Yöntem: Tüm başlık bileşikler spektroskopik ve elemental analiz ışığında yapısal olarak aydınlatıldı. Antibakteriyel tarama 'cup-plate' metodu kullanılarak yapıldı. Her bileşiğin inhibisyon zonu (mm) belirlendi ve standart ilaçla karşılaştırıldı. Bulgular: Değişken grup ve bileşiğin biyolojik aktivitesi arasındaki ilişki tartışıldı. Tartışma: Tüm bileşikler orta düzey anti bakteriyel etkinlik gösterirken; VIIa, VIIb ve VIIc daha iyi anti bakteriyel etkinlik göstermişler ve VIId, VIIe ve VIIf diğer başlık bileşiklerden daha güçlü anti fungal ajanlar olarak bulunmuşlardır.

**Anahtar Kelimeler**

Mannik Bazlar; Sentez; Karakterizasyon; Antimikrobiyal Aktivite

**Abstract**

Aim: To design, synthesize and characterize a new series of 7-(4-((substituted)-5-thioxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl)-4-(phenylamino)-9-(trichloromethyl)-1-thia-4,7,8-triazaspiro[4.4]non-8-ene-3,6-di one and evaluate for antimicrobial activity. Material and Method: All title compounds were structurally elucidated on the basis of spectroscopic and elemental analysis. The antimicrobial screening was carried out by employing cup plate method. The zone of inhibition (mm) of each compound was determined and compared with that of standard drug. Results: The relationship between the substituent group and the biological activity of the compounds was discussed. Discussion: While all the compounds exhibited moderate antibacterial activity, VIIa, VIIb and VIIc were found to be better antibacterial agents and VIId, VIIe and VIIf were found to be superior antifungal agents than the other title compounds.

**Keywords**

Mannich Bases; Synthesis; Characterization; Antimicrobial Activity

DOI: 10.4328/JCAM.2447 Received: 30.03.2014 Accepted: 28.04.2014 Printed: 01.01.2016 J Clin Anal Med 2016;7(1): 14-7
Corresponding Author: B. Santosh Kumar, Sri Krishnadevaraya University, Anantapur, A.P., India.
T.: 91 94410 17151 E-Mail: besnantosh1985@gmail.com

## Introduction

Heterocycles containing nitrogen, oxygen and sulphur atoms are time-honored because of their remarkable biological and pharmacological applications [1, 2]. Thiazolidinone is a heterocycle that has sulfur, nitrogen and carbonyl group at positions 1, 3 and 4 respectively and represents a ubiquitous scaffold in drug discovery with exceptional pharmacological applications. The antibacterial activity of thiazolidinones is due to its inhibitory activity of enzyme MurB which is a precursor during the biosynthesis of peptidoglycan [3]. It was reported that the thiazolidinone scaffold mimicked the diphosphate and different groups present around the ring generates the specificity [4, 5]. Certain thiazolidinones were recently reported to be the inhibitors of mycobacterial rhamnose synthetic enzymes [6]. On the other hand, 1,3,4-oxadiazole is a privileged structure, that bestows its derivatives with broad and potent biological functions. The derivatives of 1,3,4-oxadiazoles have been used as pharmacophores due to their favorable metabolic profile and ability to engage in hydrogen bonding [7]. The diverse pharmacological activities of both these moieties are widely exploited [8-20] as they are not only synthetically important but also possess a wide range of promising pharmacological activities. Keeping this in view, the authors have outlined simple and maneuverable synthetic methodologies for drugs containing 4-thiazolidinone and 1,3,4-oxadiazole scaffolds and evaluated for their antimicrobial activitiy.

## Material and Method

All chemicals and reagents were procured from Merck India Limited. Melting points were determined in open capillary tubes and were uncorrected (in degree Celsius). Infrared spectra of the compounds were recorded in KBr discs on FT-IR spectrometer manufactured by Perkin-Elmer. The $^1$H NMR spectra were recorded on a JOEL (300 MHz) spectrometer using TMS as an internal standard. The chemical shifts were reported in ppm scale. $^{13}$C NMR spectrometer (300 MHz) manufactured by Bruker Avance was used for recording $^{13}$C NMR spectra. The standard bacterial and fungal strains were procured from National Centre for Cell Science (NCCS), Pune, India.

### *Experimental*

The compound V was synthesized by the procedure reported in the literature [21].

Synthesis of 4-(phenylamino)-7-((5-thioxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl)-9-(trichloromethyl)-1-thia-4,7,8-triazaspiro[4.4]non-8-ene-3,6-dione (6)

A mixture of (5) (19.9g, 0.1 M), KOH (5.5g, 0.1M) ethanol (100 mL) and carbon disulphide (6.02 mL, 0.1 M) taken in a round bottomed flask equipped with a chilled water condenser was refluxed on an oil bath till the evaluation of hydrogen sulphide was stopped. Excess of alcohol was removed by distillation. The reaction mixture was cooled to room temperature, poured into ice cold water and neutralized with dilute hydrochloric acid. The solid precipitated was filtered, washed thoroughly with water, dried and recrystallized from ethanol-dioxane mixture (1:1) to give 6.

Synthesis of 7-(4-((substituted)-5-thioxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl)-4-(phenylamino)-9-(trichloromethyl)-1-thia-4,7,8-triazaspiro[4.4]non-8-ene-3,6-dione (7a-f)

A solution of 6 (0.01M) in absolute ethanol and dioxane mixture (1:1, 20 mL) was treated with formaldehyde (40%, 1.5 mL). A solution of appropriate amine (0.01 M) in ethanol (10 mL) was added to the mixture and stirred over night at room temperature. The precipitated Mannich base was collected by filtration, dried and recrystallized from ethanol-DMF (1:1)

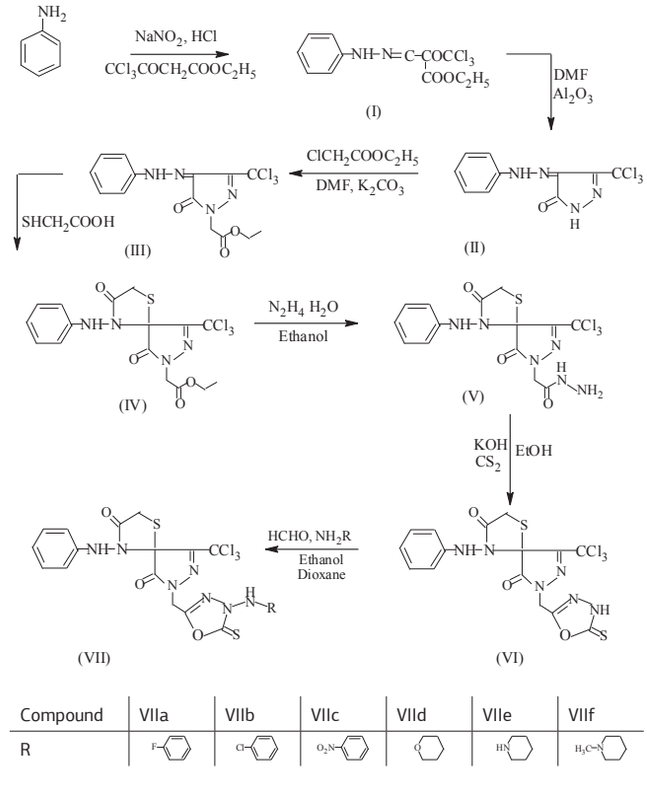
### *Characterisation of synthesized compounds*

### *Characterization of 6*

6: Yield: 70; m.p.: 140-1oC; Molecular formula: $C_{15}H_{11}Cl_3N_6O_3S_2$; Elemental analysis: Found (calculated %) C 36.44 (36.49), H 2.29 (2.25), N 17.07 (17.02); The IR(KBr, cm$^{-1}$) spectrum of 6 shows the peaks around 3125, 1722 & 1245, 1637 & 1229 and 1247 corresponding to Ar-H, characteristic peaks for thiazolidine, characteristic peak for 1,3,4-oxadiazole and C=S respectively. The $^1$H NMR (300 MHz, ppm ) spectrum of 6 recorded in DMSO-$d_6$ showed signals at 3.89 (s, 2H, $NCH_2$), 3.92 (d, 1H, -$CH_2$ of Thiazolidine attached to –S), 3.80 (d, 1H, -$CH_2$ of Thiazolidine attached to -S), 11.69 (s, H, Ar-NH), 7.29(s, 1H, NH of oxadiazole), 6.79 -8.28 (m, 4H, $C_6H_4$).

Compound: Yield; m.p.$^o$C; Molecular formula; Element Calculated% (Found%); IR vmaxin Group cm$^{-1}$; $^1$HNMR (300 MHz) δ ppm; $^{13}$C NMR (300 MHz) δ ppm.

7a: 65; 182-3; $C_{22}H_{17}Cl_3FN_7O_3S_2$; C 42.79 (42.83) , H 2.74 (2.78),




Scheme1. Synthesis of 7-(4-((substituted)-5-thioxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl)-4-(phenylamino)-9-(trichloromethyl)-1-thia-4,7,8-triazaspiro[4.4]non-8-ene-3,6-dione (7a-f)

Characterization of 7-(4-((substituted)-5-thioxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl)-4-(phenylamino)-9-(trichloromethyl)-1-thia-4,7,8-triazaspiro[4.4]non-8-ene-3,6-dione (7a-f)

N 15.84 (15.89); N-H of Mannich Product 3324, Characteristic peaks of thiazolidine 1717 & 1257, Characteristic peak for 1,3,4-oxadiazole 1641 & 1225, C=S 1261; 3.81 (s, 2H, $NCH_2$), 3.82(d,1H,-$CH_2$ of Thiazolidin attached to –S), 3.91(d, 1H, -$CH_2$

of Thiazolidine attached to –S), 4.22 (s, 1H, attached to 4-flourobenzene), 4.39(s, 2H, $CH_2$ attached to oxadiazole ring), 11.29 (s, H, Ar – NH), 7.29(s, 1H, NH of oxadiazole), 6.91 -7.49 (m, 9H, $C_6H_4$ and $C_6H_4$ of two phenyl groups); 152.1, 112.3, 125.6, 125.9, 123.4, 165.1, 31.9, 63.4, 173.3, 154.1, 84.1, 56.1, 154.9, 178.3, 71.7, 144.9, 119.5, 119.4, 155.9 and these signals are due to at $C_1$,$C_{2\&2}$',$C_{3\&3}$',$C_4$,$C_5$,$C_6$,$C_7$,$C_8$, $C_9$, $C_{10}$,$C_{13}$,$C_{15}$,$C_{16\&16}$', $C_{17\&17}$', $C_{18}$ carbon atoms respectively.

7b: 62; 187-8; $C_{22}H_{17}Cl_4N_7O_3S_2$; C 41.68 (41.72), H 2.69 (2.71), N 15.42 (15.48); N-H of Mannich Product 3331, Characteristic peaks of thiazolidine 1724 & 1259, Characteristic peak for 1,3,4-oxadiazole 1646 & 1231, C=S 1273; 3.77 (s, 2H, $NCH_2$), 3.88(d,1H,-$CH_2$ of Thiazolidine attached to –S), 3.96(d,1H,-$CH_2$ of Thiazolidine attached to –S), 4.19 (s, 1H, attached to 4-chloro benzene), 4.34 (s, 2H, $CH_2$ attached to oxadiazole ring), 11.20 (s, H, Ar – NH), 7.2(s, 1H, NH of oxadiazole), 6.71 -7.32 (m, 9H, $C_6H_4$ and $C_6H_4$ of two phenyl groups); 149.9, 111.9, 124.4, 124.9, 121.3, 164.8, 30.9, 63.9, 172.9, 153.4, 83.8, 55.9, 153.3, 177.3, 70.6, 144.2, 116.7, 128.9, 126.4 and these signals are due to at $C_1$,$C_{2\&2}$',$C_{3\&3}$',$C_4$,$C_5$,$C_6$,$C_7$,$C_8$, $C_9$, $C_{10}$,$C_{13}$,$C_{15}$,$C_{16\&16}$', $C_{17\&17}$', $C_{18}$ carbon atoms respectively.

7c: 68; 193-5; $C_{22}H_{17}Cl_3N_8O_5S_2$; C 41.08 (41.04), H 2.61 (2.66), N 17.41 (17.40); N-H of Mannich Product 3329, Characteristic peaks of thiazolidine 1728 & 1253, Characteristic peak for 1,3,4-oxadiazole 1651 & 1232, C=S 1276; 3.81 (s, 2H, $NCH_2$), 3.96 (d, 1H, -$CH_2$ of Thiazolidin attached to –S), 3.89(d, 1H, -$CH_2$ of Thiazolidine attached to –S), 4.29 (s, 1H, attached to 4-chloro benzene), 4.35(s, 2H, $CH_2$ attached to oxadiazole ring), 11.16 (s, H, Ar – NH), 7.26(s, 1H, NH of oxadiazole), 6.75 -7.49 (m, 9H, $C_6H_4$ and $C_6H_4$ of two phenyl groups); 151.3, 113.4, 126.6, 124.6, 121.9, 165.8, 31.2, 64.2, 172.8, 154.6, 85.4, 55.7, 155.6, 177.6, 70.9, 155.9, 113.4, 126.1, 135.1 and these signals are due to at $C_1$,$C_{2\&2}$',$C_{3\&3}$',$C_4$,$C_5$,$C_6$,$C_7$,$C_8$, $C_9$, $C_{10}$,$C_{13}$,$C_{15}$,$C_{16\&16}$', $C_{17\&17}$', $C_{18}$ carbon atoms respectively.

7d: 60; 188-9; $C_{20}H_{20}Cl_3N_7O_4S_2$; C 41.60 (40.51), H 3.39 (3.40), N 16.61 (16.54); N-H of Mannich Product 3311, Characteristic peaks of thiazolidine 1729 & 1255, Characteristic peak for 1,3,4-oxadiazole 1654 & 1237, C=S 1258; 3.84 (s, 2H, $NCH_2$), 3.75(d,1H,-$CH_2$ of Thiazolidine attached to –S), 4.01(d,1H,-$CH_2$ of Thiazolidine attached to –S), 4.39 (s, 1H, attached to N-methylpipyridine ring), 3.97(s, 2H, $CH_2$ attached to oxadiazole ring), 11.31 (s, H, Ar – NH), 7.29(s, 1H, NH of oxadiazole), 6.76 -7.38 (m, 5H, $C_6H_5$), 3.61 & 3.42(t, 4H, O-$CH_2$ of pyron ring), 1.72 & 1.46(q, 4H, N-C-$CH_2$ of pyron ring), 2.56(m, 1H, CH of pyron ring attached to NH); 151.7, 113.7, 128.1, 126.5, 122.1, 166.8, 31.6, 64.6, 173.5, 155.5, 85.9, 55.9, 156.6, 176.9, 66.9, 50.6, 37.5, 65.1 and these signals are due to at $C_1$,$C_{2\&2}$',$C_{3\&3}$',$C_4$,$C_5$,$C_6$,$C_7$,$C_8$, $C_9$, $C_{10}$,$C_{13}$,$C_{15}$,$C_{16\&16}$', $C_{17\&17}$'carbon atoms respectively.

7e: 71; 201-2; $C_{21}H_{22}Cl_3N_{703}S_2$; C 43.71 (43.68), H 3.80 (3.75), N 16.53 (16.59); N-H of Mannich Product 3311, Characteristic peaks of thiazolidine 1722 & 1225, Characteristic peak for 1,3,4-oxadiazole 1645 & 1232, C=S 1259; 3.65 (s, 2H, $NCH_2$), 3.67(d,1H,-$CH_2$ of Thiazolidin attached to –S), 3.59(d,1H,-$CH_2$ of Thiazolidine attached to –S), 4.10 (s, 1H, N-CH attached to piperidine ring), 3.96(s, 2H, $CH_2$ attached to oxadiazole ring), 11.21 (s, H, Ar – NH), 6.50 -7.17 (m, 5H, $C_6H_5$), 2.65 & 1.66(m, 8H, 4$CH_2$ of piperidine), 2.39(m, 1H, CH of piperidine NH); 151.0, 113.7, 127.8, 127.1, 122.3, 167.1, 31.2, 63.8, 172.9, 155.1, 86.1, 56.1, 155.1, 177.3, 70.1, 154.9, 113.9, 126.4, and these signals are due to at $C_1$,$C_{2\&2}$',$C_{3\&3}$',$C_4$,$C_5$,$C_6$,$C_7$,$C_8$, $C_9$, $C_{10}$,$C_{13}$,$C_{15}$,$C_{16\&16}$', $C_{17\&17}$' carbon atoms respectively.

7f: 65; 206-7; $C_{21}H_{23}Cl_3N_{803}S_2$; C 41.66 (41.62), H 3.89 (3.83), N 18.53 (18.49); N-H of Mannich Product 3312, Characteristic peaks of thiazolidine 1728 & 1252, Characteristic peak for 1,3,4-oxadiazole 1646 & 1239, C=S 1257; 3.69 (s, 2H, $NCH_2$), 3.69(d,1H,-$CH_2$ of Thiazolidine attached to –S), 3.65(d,1H,-$CH_2$ of Thiazolidin attached to –S), 4.03 (s, 1H, attached to N-methylpipyridine ring), 3.97(s, 2H, $CH_2$ attached to oxadiazole ring), 11.25 (s, H, Ar – NH), 6.55 -7.25 (m, 5H, $C_6H_5$), 2.55 & 2.36(t, 4H, N-$CH_2$ of N-methyl piperidine ring), 1.76 & 1.56(q, 4H, N-C-$CH_2$ of N-methyl piperidine ring), 2.76(m, 1H, CH of N-methyl piperidine ring attached to NH); 151.1, 112.6, 128.1, 127.9, 122.1, 167.1, 32.4, 64.2, 172.7, 155.3, 86.4, 57.1, 157.9, 177.7, 66.8, 56.9, 31.2, 54.5, 46.8 and these signals are due to at $C_1$,$C_{2\&2}$',$C_{3\&3}$',$C_4$,$C_5$,$C_6$,$C_7$,$C_8$, $C_9$, $C_{10}$,$C_{13}$,$C_{15}$,$C_{16\&16}$', $C_{17\&17}$' $C_{18}$ carbon atoms respectively.

## Results and Discussion

Condensation of [5-Oxo-4-(4-substituted aryl hydrazono)-3-trichloromethyl-4, 5-dihydro- pyrazol- 1-yl]-acetic acid hydrazide (5) with a mixture of KOH, ethanol and carbon disulphide afforded compound 6 in good yield. Compound 6 was subjected to Mannich reaction with *p*-fluorophenylamine in the presence of a solution of formaldehyde in ethanol-dioxane mixture to give 7-((4-(((4-flourophenyl)amino)methyl)-5-thioxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl)-4-(phenylamino)-9-(trichloromethyl)-1-thia-4,7,8-triazaspiro[4.4]non-8-ene-3,6-dione (7a). Treatment of 6 with *p*-chloro phenyl amine/*p*-anisyl amine/ *p*-nitro phenyl amine/ terahydro-pyran-4-ylamine / piperidine-4-ylamine / 1-methyl-piperidin-4-ylamine afforded the respective Mannich base (7b–f). The compounds were characterized by elemental analysis, IR, $^1$H NMR and $^{13}$C NMR spectral data. While the spectral data have confirmed the presence of characteristic groups, elemental analysis data for C, H, and N were within ±0.5% of the theoretical values. The Mannich bases under study were screened for their antimicrobial activity by cup plate method [22]. The bacteria screened were *Staphylococcus aureus* NCCS 2079, *Bacillus cereus* NCCS 2106, *Escherichia coli* NCCS 2065 and *Pseudomanas aeruginosa* NCCS 2200 and the fungi screened were *Aspergillus niger* NCCS 1196 and *Candida albicans* NCCS 2106. Ciprofloxacin and Clotrimazole were used as standards (10 µg/mL) for antibacterial studies and antifungal studies respectively. The details are given in the Table 1. In order to analyze the impact of the nature of R on the antimicrobial activity, derivatives incorporating *p*-fluoro phenyl, *p*-chloro phenyl, *p*-nitro phenyl, tetrahydrapyran, piperydinyl, N-methyl piperydinyl were synthesized. The Mannich bases containing electron with drawing substituents at the 4 position of phenyl ring has shown good antibacterial activity where the Mannich bases containing tetrahydrapyran, piperydinyl, N-methyl piperydinyl have shown good antifungal activity. The higher activity of morpholinyl derivative in comparison to piperydinyl derivative is due to the fact that the potential oxygen atom of the morpholine can participate in the formation of hydrogen bonds in the drug-target site.

Table 1. Zone of inhibition from antimicrobial activity studies

| Compound (20 µg/mL) | Zone of inhibition (mm)* | | | | | |
|---|---|---|---|---|---|---|
| | Bacteria screened | | | | Fungi screened | |
| | *Staphylococus aureus* NCCS 2079 | *Bacillus Cereus* NCCS 2106 | *Escherichia coli* NCCS 2065 | *Pseudomanas aeruginos* NCCS 2200 | *Aspergillus niger* NCCS 1196 | *Candida albicans* NCCS 2106 |
| VIIa | 18 | 17 | 19 | 17 | 16 | 14 |
| VIIb | 21 | 19 | 21 | 18 | 18 | 14 |
| VIIc | 22 | 20 | 23 | 21 | 20 | 21 |
| VIId | 17 | 18 | 19 | 16 | 22 | 24 |
| VIIe | 16 | 15 | 14 | 16 | 17 | 18 |
| VIIf | 14 | 16 | 18 | 15 | 20 | 23 |
| Ciprofloxacin | 25 | 23 | 27 | 22 | -- | -- |
| Clotrimazole | -- | -- | -- | -- | 26 | 28 |

### *Conclusion*

A series of novel Mannich bases incorporating 4-thiazolidinone and 1,3,4-oxadiazole moieties were synthesized and characterized by FTIR, $^{1}H$ NMR, $^{13}C$ NMR spectroscopic analysis and elemental analysis. The title compounds were evaluated for their in vitro antimicrobial activity against six bacteria including two gram positive, two gram negative and two fungal strains. Among compounds screened, VIIa, VIIb and VIIc (VIIc > VIIb > VIIa) were found to be better antibacterial agents compared to VIId, VIIe and VIIf (VIId > VIIf > VIIe) which were found to be superior antifungal agents.

### *Competing interests*

The authors declare that they have no competing interests.

**References**


1. Brown BA, Wallace Jr. RJ, Onyi GO. Activities of clarithromycin against eight slowly growing species of nontuberculous mycobacteria, determined by using a broth microdilution MIC system. Antimicrob. Agents Chemother. 1992;36:1987-90.
2. El-Kashef HS, Abd-Alla MA, Bayoumi BE, El-Timawy AAM. Synthesis and antibacterial activity of some new pyrazolone dyes. J Chem Technol Biot. 1983;33:294-98.
3. Bronson JJ, DenBleyker KL, Falk PJ, Mate RA, Ho HT, Pucci MJ, Snyder LB. Discovery of the first antibacterial small molecule inhibitors of MurB. Bioorg. Med. Chem. Lett.2003;13: 873-5.
4. Verma A, Saraf SK. 4-Thiazolidinone-A biologically active scaffold. Eur. J. Med. Chem.2008;43:897-905.
5. Bonde CG, Gaikwad NJ. Synthesis and preliminary evaluation of some pyrazine containing thiazolines and thiazolidinones as antimicrobial agents. Bioorg. Med. Chem. 2004;12:2151-61.
6. Babaoglu K, Page MA, Jones VC, McNeil MR, Dong C, Naismith JH, Lee RE. Novel inhibitors of an emerging target in Mycobacterium tuberculosis; substituted thiazolidinones as inhibitors of dTDP-rhamnose synthesis. Bioorg. Med. Chem. Lett., 2003;13:3227-30,
7. Polshettiwar V, Varma RS. Greener and rapid access to bio-active heterocycles: one-pot solvent-free synthesis of 1,3,4-oxadiazoles and 1,3,4-thiadiazoles. Tetrahedron Letters 2008;49:879-83.
8. Havrylyuk D, Mosula L, Zimenkovsky B, Vasylenko O, Gzella A, Lesyk R. Synthesis and anticancer activity evaluation of 4-thiazolidinones containing benzothiazole moiety. Eur J Med Chem. 2010;45:5012–21.
9. Rawal RK, Solomon VR, Prabhakar YS, Katti SB, De Clercq E. Synthesis and QSAR studies on thiazolidinones as anti-HIV agents. Comb Chem High Throughput Screen. 2005;8:439-43.
10. Pathak RB, Chovatia PT, Parekh HH. Synthesis, antitubercular and antimicrobial evaluation of 3-(4-chlorophenyl)-4-substituted pyrazole derivatives. Bioorg Med Chem Lett. 2012;22:5129–33.
11. Shiva NM, Srinivasa V. Screening of new synthetic thiazolidine-4-ones for anti inflammatory activity in albino rats. Indian J Pharmacol. 2003;35:61–62.
12. Mohamed MS, Kamel MM, Kassem EM, Abotaleb N, Abd El-Moez SI, Ahmed MF. Novel 6,8-dibromo-4 (3H) quinazolinone derivatives of antibacterial and antifungal activities. Eur J Med Chem. 2010;45:3311–9.
13. Arey BJ, Yanofsky SD, Claudia Pérez M, Holmes CP, Wrobel J, Gopalsamy A, Stevis PE, López FJ, Winneker RC. Differing pharmacological activities of thiazolidinone analogs at the FSH receptor. Biochem Biophys Res Commun. 2008;368:723-8.
14. Taranalli AD, Bhat AR, Srinivas S, Saravanan E. Antiinflammatory, Analgesic and Antipyretic Activity of Certain Thiazolidinones. Indian J Pharm Sci. 2008;70:159–164.
15. El-Sayed WA, El-Essawy FA, Ali OM, Nasr BS, Abdalla MM, Abdel-Rahman AA. Anti-HIV activity of new substituted 1,3,4-oxadiazole derivatives and their acyclic nucleoside analogues. Z Naturforsch C. 2009;64:773-8.
16. Kaplancikli ZA, Altintop MD, Turan-Zitouni G, Ozdemir A, Ozic R, Akalin G. Synthesis, antimicrobial activity and cytotoxicity of novel oxadiazole derivatives. J Enzyme Inhib Med Chem. 2012; 27:51-7.
17. Shashikant RP, Rabara PA, Jayashri SP, Bukitagar AA, Wakale VS, Musmade DS. Synthesis and evaluation of some novel substituted 1,3,4-oxadiazole and pyrazole derivatives for antitubercular activity. Indian Journal of Chemistry. 2009;48B:1453-56 .
18. Shivarama Holla B, Poojary KN, Subrahmanya Bhat K, Ashok M, Poojary B. Synthesis and anticancer activity studies on some 2-Chloro-1, 4-bis-(-substituted-1, 3, 4-oxadiazole-2-ylmethyl enoxy) phenylene derivatives. Indian J Chem. 2005;44B:1669–73.
19. Ronad PM, Hunashal RD, Darbhamalla S, Maddi VS. Synthesis and evaluation of anti-inflammatory and analgesic activities of a novel series of substituted-N-(4-methyl-2-oxo-2H-chromen-7-yl) benzamides. Arzneimittelforschung. 2008;58:641-6.
20. Khan MT, Choudhary MI, Khan KM, Rani M, Atta-ur-Rahman. Structure-activity relationships of tyrosinase inhibitory combinatorial library of 2,5-disubstituted-1,3,4-oxadiazole analogues. Bioorg Med Chem. 2005;13:3385-95.
21. Ranga Raju Kakarlapudi, Raghavendra Guru Prasad Aluru, Santosh Kumar Badampudi, Ravindranath Lakshmana Rao Krishna Rao. Antimicrobial evaluation of Mannich bases carrying Azetidinone moiety, Accepted by Journal of Analytical and Clinical Medicine.
22. Rose SB, Miller RB. Studies with the Agar Cup-Plate Method. I. A Standardized Agar Cup-Plate Technique. J Bacteriol. 1939;38:525–537.



***How to cite this article:***

Ranga Raju K, Santosh Kumar B, Guru Prasad AR, Ravindranath LK. Synthesis and Antimicrobial Activity of Novel Heterocycles Containing Thiazolidinone and 1,3,4-Oxadiazole Moieties. J Clin Anal Med 2016;7(1): 14-7.